



Comparative Study of Bone Marrow Aspirate and Bone Marrow Trepine Biopsy Findings in Lymphomas

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Abstract

Background and Objective: Bone marrow biopsy is an integral part of staging work-up and prognostication for Hodgkin and non-Hodgkin lymphoma (NHL). Objective of this study is to study and compare the diagnostic findings of aspirates and trephine biopsies in lymphomas.

Methods: A prospective study was conducted on sixty two cases of Bone marrow aspirates and trephine biopsies from biopsy proven lymphomas (Hodgkins and Non Hodgkins Lymphoma) for the period of eighteen months from February 2016 to August 2017. Bone marrow biopsies were taken with Jamshidi needle. Trepines were fixed in 10% buffered formalin for 24 hours and then placed in a decalcifying medium (EDTA Tris buffer) for 2 days at room temperature. The serial sections were stained by hematoxylin and eosin and reticulin stains. The bone marrow aspirates and peripheral smears were stained using Leishman stain.

Results and Discussion: The study included 6 cases of Hodgkins lymphoma and 56 cases of Non Hodgkin lymphomas. Median age of presentation was 55.2 years. Male: female ratio of 3.4: 1 was observed. A total of 22 cases (35.5%) showed lymphoma infiltrating the bone marrow. The most common pattern of involvement in the study is diffuse pattern (31.8%), followed by mixed pattern (22.7%), focal pattern (18.2%), paratrabecular pattern(9%), interstitial pattern(9%) and nodular pattern of involvement(9%). 10 out of 22 bone marrow positive cases showed fibrosis in the trephine biopsy(45%). The highest incidence of marrow involvement was noted in CLL/SLL, hairy cell leukemia (100%), followed by DLBCL(45%) and follicular lymphoma(43%). Atypical lymphoid cells were seen in the bone marrow aspirate in 11 out of 22 cases (50%) that showed marrow involvement in trephine biopsy. 9 out of 62 cases (15%) showed circulating tumour cells in the peripheral blood.

Conclusion: Lymphomas in the bone marrow trephine have characteristic infiltration patterns specific to different subtypes of lymphomas. Additional finding like fibrosis is frequent in bone marrow with lymphoma infiltration. The bone marrow aspirate helps in better appreciation of atypical lymphoid cells. Patient with lymphoma should undergo Bone marrow trephine biopsy because of its higher sensitivity compared to Bone marrow aspirate.

Keywords: Bone marrow aspirate; bone marrow trephine; lymphoma infiltration; patterns of involvement; fibrosis.

Introduction

Bone marrow biopsy is a routine investigation in the diagnosis and staging of Hodgkins disease and Non Hodgkins lymphoma and it has prognostic significance.¹ It is considered essential at the time of diagnosis before starting chemotherapy as well as after therapy for assessing response² Marrow involvement in addition to nodal disease is indicative of stage IV disease in Ann Arbor staging of Lymphomas.³ Bone marrow, an organ of lymphopoiesis, normally contains up to 20-35% lymphocytes. They are either diffusely dispersed or formed as nodular lymphoid aggregates. Most of the lymphoid infiltrates can be considered as either reactive or neoplastic based on their extent of involvement, distribution, cytological findings and immunophenotype.

Objectives of the Study

1. To study the morphological findings of lymphomas in bone marrow aspirates and trephine biopsies.
2. To compare bone marrow aspirate versus bone marrow trephine biopsy in detecting lymphoma infiltration in the marrow.

Materials and Methods

Sixty two cases of Bone marrow aspirates and trephine biopsies from biopsy proven lymphomas (Hodgkins and Non Hodgkins Lymphoma) were selected from the period of eighteen months from February 2016 to August 2017.

Peripheral smear, Bone marrow aspirate and biopsy findings were studied. All marrow positive and negative reports (no marrow involvement) were included in the study results.

1. The following data were collected based on the proforma prepared:-

- Distribution/Pattern
- Abnormal cells
- Fibrosis
- Necrosis
- IHC (as needed)
- Normal marrow

2. Leishman stain was done on the peripheral smear and bone marrow aspirate smears.

3. Bone marrow biopsies were taken with Jamshidi needle. Trepines were fixed in 10% buffered formalin for 24 hours and then placed in a decalcifying medium for 2 days at room temperature. The decalcifying fluid was changed daily.

The decalcifying medium used is 10g of Ethylene Diamine Tetra acetate disodium salt and 3.3 g of tris buffer (Hydroxy methyl Aminoethane) were dissolved in distilled water to obtain final volume of 100 ml.

The bone marrow specimens after decalcification were processed and paraffin embedded and 5 micron thick sections were prepared. Hematoxylin and Eosin stain were done routinely in all cases.

4. Relevant IHC markers were done in selected cases that include: LCA, CD3, CD10, CD34, CD5, Bcl2, CD15, CD30 and Tdt.

Statistical Analysis: All data were entered in Microsoft excel and appropriate statistical tests were applied.

Observations

In the present study conducted at Department of Pathology, Government Medical College Thiruvananthapuram;

1. 62 cases of lymphomas were studied in this descriptive study; cases were selected based on their lymph node diagnosis whose bone marrow study were being done for staging and assessing response.

2. The study included 6 cases of Hodgkins lymphoma and 56 cases of Non Hodgkin lymphomas.

3. The Non Hodgkin lymphomas in the study were diffuse large B cell lymphoma, small cell lymphoma, marginal zone lymphoma, follicular lymphoma, mantle cell lymphoma, T cell lymphoma and hairy cell leukemia.

4. Median age of presentation was 55.2 years.

5. Sex ratio of 3.4 : 1 was observed.

6. Peripheral smear involvement:-

9 out of 62 cases (15%) showed circulating tumour cells in the peripheral blood. The cases that showed circulating tumour cells are CLL/SLL, Follicular lymphoma and hairy cell leukemia.

2 out of 6 cases of Hodgkin's lymphoma showed marked eosinophilia in the peripheral blood.

7. Bone marrow aspirate:

Atypical lymphoid cells were seen in the bone marrow aspirate in 11 out of 62 cases in the study (17.7%) and out of 22 cases (50%) that showed marrow trephine involvement.

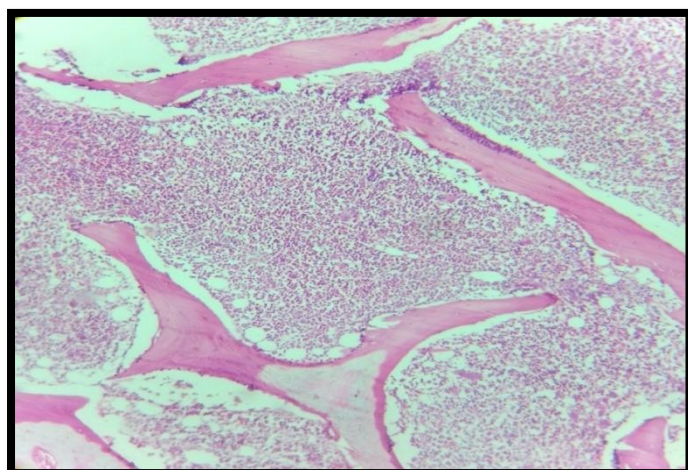
Cell characteristics specific to certain subtypes of lymphomas noted were the following:

- Buttock shaped cleaved cells in Follicular lymphoma; (2/7 cases)
- mature lymphocytes in CLL/SLL; (6/6 cases)
- large lymphoid cells in DLBCL (2/20 cases) and
- hairy cells in hairy cell leukemia.(1/1 case)

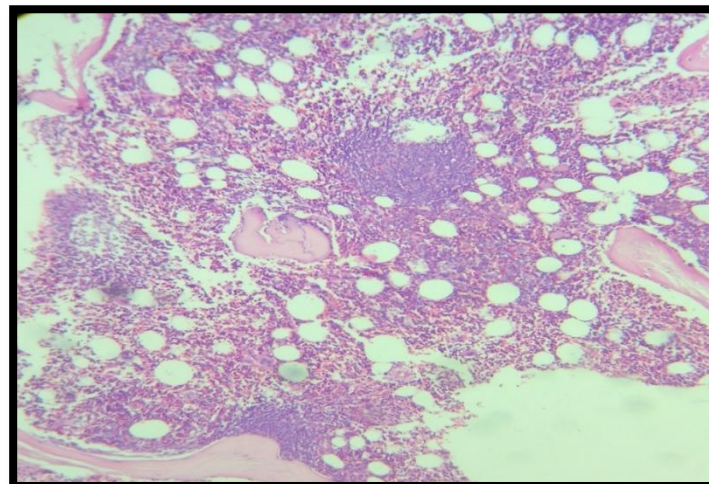
8. Bone marrow trephine biopsy:

o A total of 22 cases (35.5%) showed lymphoma infiltrating the bone marrow.

- The most common pattern of involvement^{4,5} in the study is diffuse pattern (31.8%), followed by mixed pattern (22.7%), focal pattern(18.2%), paratrabeular pattern (9%), interstitial pattern (9%) and nodular pattern of involvement (9%).



BMT showing diffuse infiltration in DLBCL (100x)



BMT showing mixed pattern in FL(400x)

- 10 out of 22 bone marrow positive cases showed fibrosis in the trephine biopsy. (45%)

- None of the cases analysed in the study showed marrow necrosis.

9. Small lymphocytic lymphoma showed the maximum marrow involvement (6/6) in this study along with hairy cell leukemia (1/1), and followed by DLBCL (9/20), follicular lymphoma (3/7), Hodgkin's lymphoma (2/6) and marginal zone lymphoma(1/9).

10. Of the 62 samples studied 40 cases showed normal marrow study.(64.5%)

11. The sensitivity and specificity of Bone marrow aspirate in the present study was 50% and 100% respectively and the overall diagnostic accuracy of BMA in the present study is 82.86%. This gives the BMA a lower sensitivity in detecting lymphoma involvement in comparison to trephine biopsy.

Discussion

In my study, 62 cases of lymphomas (both Hodgkin and Non Hodgkin lymphoma) were studied.

Pattern of Involvement: In my study the most frequent pattern noted is- diffuse pattern (31.8%), followed by mixed pattern (22.7%), focal pattern (18.2%), paratrabeular pattern (9%), interstitial pattern (9%) and nodular pattern of involvement (9%). In a study conducted by Kaur et al⁶, most common pattern of involvement was mixed (36%)

followed by diffuse (27%), interstitial (24%) and nodular (12%). In a study conducted by Kumar et al, the predominant histological pattern noted was mixed (51.85%), followed by focal non-paratrabeular (22.2%), paratrabeular (11.1%), diffuse (7.5%) and interstitial (7.5%). Hence comparing with various studies we arrive at a conclusion that 4 common patterns of bone marrow infiltration are: Mixed, diffuse, focal and paratrabeular patterns.

Fibrosis: In this study, 10 out of 22 bone marrow positive cases showed fibrosis in the trephine biopsy. (45%). Fibrosis is quite common in marrow involvement of the lymphomas.

Necrosis: No cases in the study showed marrow necrosis.

Incidence of Bone Marrow Involvement in Various Histologic Subtypes

The highest incidence of marrow involvement was noted in CLL/SLL, hairy cell leukemia (100%) followed by DLBCL(45%) and follicular lymphoma (43%). Hodgkins lymphoma showed 33% and MZL -11%. In a study conducted by Kaur et al, CLL/SLL showed maximum marrow involvement (70%) followed by DLBCL (17%). In a study conducted by Kumar et al, DLBCL showed the maximum involvement followed by T cell lymphoma, Follicular lymphoma and small cell lymphoma.

The findings in other studies are in agreement with my study.

Table 19: Bone marrow aspirate in predicting lymphoma infiltration when trephine biopsy is gold standard(2)

Sensitivity	50%
Specificity	100%
Positive Predictive value	100%
Negative Predictive value	78.4%

An accuracy of 82.86% was obtained in this study.

The present study showed comparable results with other similar studies.

Conclusion

- Lymphomas in the bone marrow trephine have characteristic infiltration patterns specific to different subtypes of lymphomas.
- Additional finding like fibrosis is frequent in bone marrow with lymphoma infiltration.
- The bone marrow aspirate helps in better appreciation of atypical lymphoid cells.
- Patient with lymphoma should undergo Bone marrow trephine biopsy because of its higher sensitivity compared to Bone marrow aspirate.

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